Gwenaelle (Gwen) Geleoc is an Assistant Professor at Boston Children’s hospital and Harvard Medical School. She received her PhD from the University of Montpellier, France. She did two postdoctoral training, the first one with Professor Jonathan Ashmore at University College London where she studied inner ear outer hair cell motility and a second one at Harvard Medical School with Professor David Corey where she studied mechano-electrical transduction in hair cells of the inner ear. Together with Dr. Jeffrey Holt, she started her laboratory at the University of Virginia and moved back to Boston, 10 years later to join the Department of Otolaryngology at Boston Children’s Hospital.

Dr. Geleoc trained as a physiologist and as an independent investigator, she studies the development of inner ear hair cells to unravel the role of deafness genes associated with hair cell function and more precisely mechano-electrical transduction and voltage dependent channels shaping the hair cell receptor potential. Over the past five years, a major portion of her work has been focused on understanding the role of Usher gene which are associated with the most common deaf-blindness syndrome, and the development of novel strategies aimed at restoring function.

Abstract

"Gene therapy restores hearing and balance in a mouse model of Usher syndrome type 1C"

Usher syndrome type 1 is associated with congenital sensorineural hearing loss, vestibular areflexia and progressive retinitis pigmentosa (RP). A recessive USH1C c.216G>A mutation, identified in French-Acadian patients, creates a cryptic splice site which reduces production of harmonin. Harmonin is essential for normal inner ear hair cell development and function. Our goal is to identify novel biological tools to treat auditory and vestibular deficits associated with this mutation.

Adeno-associated virus (AAV) gene augmentation therapy is a promising approach to target recessive mutations of genes expressed in the inner ear. An antisense oligonucleotide (ASO) that corrects the splicing defect also partially restores auditory and vestibular function in Ush1c c.216AA mouse mutants. In this report, we describe and compare results obtained with local deliveries of either therapeutic to the inner ear through the round window membrane. Our work shows that both treatments lead to recovery of Ush1c gene and protein expression along with restoration of hair cell function. This cellular repair promotes increased hair cell survival, rescues complex auditory function, and recovers hearing and balance behavior to near wild-type levels. The data represent unprecedented recovery of inner ear function. Comparative benefits and shortcomings of both treatments will be discussed.